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Observations of Cancer Incidence Surveillance in Duluth, Minnesota

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In 1973, amphibole asbestos fibers were discovered in the municipal water supply of Duluth, Minnesota. The entire city population of approximately 100,000 was exposed from the late 1950s through 1976 at levels of 1–65 million fibers per liter of water. Because of previous epidemiologic studies that linked mesothelioma, lung and gastrointestinal cancers to occupational exposure to asbestos, surveillance of cancer incidence in residents of Duluth was initiated to determine the health effect from ingestion of asbestos. The methodology of the Third National Cancer Survey (TNCS) and SEER Program was used. Duluth 1969–1971 rates were compared with TNCS rates for the cities of Minneapolis and St. Paul during 1969–1971; Duluth rates during 1974–1976 are compared with Duluth 1969–1971; Duluth rates during 1979–1980 are compared with Duluth 1969–1971 and with Iowa SEER; and a table of the occurrence of malignant mesothelioma is presented. Statistically significant excesses are observed in several primary sites in Duluth residents. However, lung cancer in Duluth females is the only primary site considered also of biological significance. The mesothelioma incidence rate is no more than expected. This paper also describes the problems of long-term surveillance of exposed populations considered at risk of environment cancer, the need for improved study methodologies and the use of federal records for follow up of exposed individuals.

Introduction

Before presenting recent findings from the surveillance of cancer incidence in Duluth, it seems appropriate to review the history of the situation and the duration and intensity of exposure to amphibole in the city, which at the time of exposure had a population of approximately 100,000.

In 1973, amphibole fibers were discovered in the municipal water supply of Duluth through studies done by the Environmental Protection Agency. A Federal Court ruling indicated that the fibers were a result of a taconite mining company dumping taconite tailings wastes into Lake Superior since 1955 (*1*). In the late 1950s, the mining company, which is located 50 miles northeast of Duluth on the lake, increased the amount dumped to approximately 67,000 tons per day, which continued into 1980. Taconite is low-grade iron ore that is mined and processed into pellets of higher grade iron ore and shipped to steel mills on the Great Lakes. This particular supply of taconite is mined from amphibole-bearing rock. Cummingtonite-grunerite is the principal amphibole in this deposit.

U.S. EPA data on Duluth water samples in 1939–1940 and 1949–1950 indicated trace amounts of fibers, but samples from 1965 contained large amounts of amphibole. It is not known when amphibole fiber levels increased to those levels. The 1973 tapwater samples collected by EPA contained 1 to 30 million amphibole fibers/L, the level generally dependent on lake weather conditions and length of time the water was in the water distribution system (*2*). In 1976, water samples were collected from 20 homes in Duluth and a range of 2 to 64 million amphibole fibers/L was found. Storm conditions in the lake have produced levels as high as 100 million fibers/L. Electron microscope studies at the Minnesota Department of Health have indicated that the physical characteristics of the fibers are: a mean length of 1.13 μm, a mean width of 0.18 μm and thus, an aspect ratio (length/width) of 6.5:1 (unpublished, Minnesota Department of Health, 1978). The aspect ratio of Duluth amphibole is double that of the OSHA arbitrary definition of a fiber with a minimum aspect ratio of 3:1.

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A water filtration plant in Duluth became operational in January 1977, removing 99.9% of the fibers. The length of exposure for Duluth residents may be considered to be 17 years, 1960–1976, and the level of exposure to be in the range of 1 to 65 million fibers/L. Until recently, monitoring of the water supply occurred daily at one of several points in the entire water distribution system.

In 1974, because of the known health risk of cancer to those occupationally exposed by inhalation to asbestos (*3–11*) and the public health concern regarding the unknown risk of those ingesting asbestos from a public water supply, a study of cancer in Duluth residents was designed to determine cancer incidence during 1969–1981.

Generally, 10–20 yr is considered the induction period for cancer of most primary sites and may be as long as 30–50 yr following asbestos exposure (*12*). Therefore, Duluth cancer incidence rates during 1969–1971, approximately 10 yr following the initiation of exposure, are considered baseline rates with which to compare the results of surveillance through time. The rates beginning in the mid-1970s would be the first rates that could reflect any possible increase in cancer due to exposure, assuming exposure began in approximately 1960.

Methods

The methodology used was that of the Third National Cancer Survey (TNCS) of 1969–1971 (*13*) and the current SEER Program at the National Cancer Institute (*14*). Personnel who worked on the Minneapolis-St. Paul component of the TNCS have conducted the study in Duluth. This has been important for the standardization and uniformity of methodology and data collection procedures and for the comparison of data between study areas.

The study requires the identification of all cancer cases in the study population through the review of hospital medical records, pathology and autopsy reports, and death certificates, and the abstracting of patient charts at the three hospitals in Duluth, the Mayo Clinic, and the University of Minnesota and Veterans Administration Hospitals in Minneapolis. The abstracted information includes name and address of patient, age, sex, race, date of diagnosis, primary site and histology, and hospital of diagnosis.

Duluth rates during 1969–1971 are compared with TNCS rates for the cities of Minneapolis and St. Paul, by using the Mantel-Haenszel method for determination of statistical significance (*15*). Minneapolis and St. Paul are considered excellent

Table 1. Characteristics of populations of Duluth and comparison cities.[a]

	Duluth	Minneapolis	St. Paul
Total population (1970 census)	100,578	434,400	309,980
Median age			
Males	27.8	27.8	26.3
Females	31.5	30.7	29.7
Birthplace			
% born in Minnesota	69.9	67.1	72.6
% foreign-born	5.2	4.8	3.9
% foreign stock (foreign-born individuals + natives of foreign or mixed parentage)	27.9	23.9	21.8
Norwegian and Swedish	10.4	9.4	4.4
German and Austrian	2.5	3.4	5.2
Finnish	2.8	0.5	0.2
% white	98.3	95.6	95.4
% who lived in same county in 1965 as in 1970	82.1	75.9	79.7
Median no. of school years completed (for population ≥ 25 yr old)	12.3	12.3	12.2
% of males ≥ 16 yr old in civilian labor force unemployed	6.0	4.2	3.6
% families below poverty level	7.4	7.2	6.4
Median family size	3.48	3.26	3.52
Median family income	$9,313	$9,960	$10,544
% in selected occupations			
Professional, technical, and kindred workers	16.4	16.5	16.5
Craftsmen, foremen, and kindred workers	13.0	10.7	11.7
Laborers except farmers	4.8	4.2	4.3
% in selected industries			
Mining	0.6	0.1	0.1
Construction	4.8	4.2	4.7
Manufacturing	16.4	20.5	25.1

[a]Based on 1970 U.S. census data.

comparison cities because of similar population characteristics. Table 1 lists data from the 1970 census and generally indicates that age, sex and race distributions and socioeconomic, occupational, and ethnic factors (all of which are associated with cancer incidence rates) are similar for the three cities. Important detailed dissimilarities are noted for the Duluth population; namely, smaller size, higher percentage of foreign stock, higher percentage of males 16 years of age and older unemployed, a sixfold excess of the population in mining industries and lower percentage in manufacturing industries. Minneapolis and St. Paul municipal water supplies are also known to have very low levels of amphibole fibers, at least an order of magnitude lower than Duluth (Minnesota Department of Health, unpublished data, 1979).

There are no existing cancer incidence data for Minneapolis and St. Paul since 1969–1971. Standardized morbidity ratios (SMRs) compare Duluth rates during the later years of the current study period of 1969–1981 with rates from the Iowa component of the SEER Program. Tests of statistical significance were performed, using a method defined by Bailar (*16*). Future analysis of the entire study period will include comparison with SEER data from selected cities of Iowa because of similar population characteristics as described above for the cities of Minneapolis and St. Paul. Those Iowa cities are known to be virtually free of amphibole fibers in their municipal water supplies (J. Millette, Health Effects Research Laboratory, U.S. EPA, personal communication).

It is important to note that the methodologies of the cancer incidence studies of Duluth, San Francisco, and Seattle (all presented at this workshop) are virtually identical. A common study methodology makes comparison of those study results quite meaningful among the three cities, all with different exposure factors.

Results

Tables 2 and 3 contain absolute numbers of Duluth cancer cases and average annual age-adjusted incidence rates of selected primary sites for males and females, respectively, in the cities

Table 2. Cancer incidence rates of selected sites, male residents of Duluth and comparison cities 1969–1971, and Duluth 1974–1976.

	Average annual age-adjusted rates per 100,000 population[a]					
	1969–1971					
	Duluth		Minneapolis	St. Paul	1974–1976, Duluth	
Primary site	Rate	Number	rate	rate	Rate	Number
All sites combined	388.0	667	375.7	362.4	361.4	617
Total gastrointestinal	109.6	191	106.8	106.8	94.4	163
Stomach	20.2	36	16.7	14.3	15.0	26
Colon, excluding rectum	34.3	60	40.8	42.6	28.5	49
Transverse colon	6.4	11	6.0	7.9	7.2	12
Descending colon	4.0	7	3.9	3.8	1.6	3
Sigmoid	7.4	13	12.9	15.2*	8.8	15
Cecum	7.9	14	10.6	8.0	7.9	14
Ascending colon	4.9	8	3.8	4.3	1.7	3
Rectum	13.8	24	13.1	17.6	21.6	37
Liver	3.2	5	3.0	2.3	0.6	1
Pancreas	16.9	30	14.2	11.8	14.4	25
Peritoneum, retroperitoneum, intra-abdominal	4.3	7	1.4*	1.5	0	0
Other peritoneum and digestive	2.8	5	0.3†	0.2†	1.1	2
Lung and bronchus	75.5	128	70.1	64.7	68.6	116
Pleura	0	0	0.3	0.4	3.1	5
Prostate	90.4	161	69.3†	68.0†	71.7*	127
Bladder	21.5	37	23.7	20.0	24.2	42
Kidney and renal pelvis	10.8	17	11.6	10.5	8.1	14
Lymphomas	8.0	13	12.4	11.1	14.1	22
Multiple myeloma	5.9	10	4.0	3.8	1.7	3
Leukemias	13.6	23	12.9	15.6	14.8	25

[a]Rates were age-adjusted using the 1970 Minnesota population as the standard.
*Statistically significant difference with Duluth 1969–1971 at $p \leq 0.05$.
†Statistically significant difference with Duluth 1969–1971 at $p \leq 0.01$.

Table 3. Cancer incidence of selected sites, female residents of Duluth and comparison cities 1969–1971, and Duluth 1974–1976.

	Average annual age-adjusted rates per 100,000 population[a]					
	1969–1971					
	Duluth		Minneapolis	St. Paul	1974–1976, Duluth	
Primary site	Rate	Number	rate	rate	Rate	Number
All sites combined	332.1	613	320.2	327.2	333.7	631
Total gastrointestinal	83.8	162	78.8	84.2	74.5	145
Stomach	9.9	19	9.3	11.8	7.8	15
Colon, excluding rectum	34.7	67	37.9	38.7	31.7	62
Transverse colon	7.7	15	5.1	5.7	4.0	8
Descending colon	1.2	2	2.5	4.4	2.0	4
Sigmoid	6.3	12	10.9	11.8*	9.2	18
Cecum	10.1	20	9.7	8.6	9.2	18
Ascending colon	4.8	9	5.7	5.3	5.2	10
Rectum	8.2	16	9.0	9.2	10.0	19
Liver	1.0	2	0.9	2.2	0	0
Pancreas	13.2	26	8.3	9.9	8.7	17
Peritoneum, retroperitoneum, intra-abdominal	0.5	1	1.2	2.6	1.1*	2
Other peritoneum and digestive	1.5	3	0.8	0.2	0.5	1
Lung and bronchus	9.3	18	14.7	12.6	17.9*	34
Pleura	0	0	0.1	0.2	0.5	1
Breast	89.9	163	90.8	78.2	85.4	162
Cervix	25.3	41	18.1	28.3	15.7	25
Corpus	27.1	53	18.9*	24.8	43.5*	84
Bladder	6.3	12	6.8	9.1	7.1	14
Kidney and renal pelvis	8.4	16	6.6	6.5	7.3	14
Lymphomas	6.1	11	9.2	10.6	11.8	22
Multiple myeloma	0.5	1	6.2†	3.1	4.2*	8
Leukemias	10.6	19	10.0	7.8	9.8	18

[a]Rates were age-adjusted using the 1970 Minnesota population as the standard.
*Statistically significant difference with Duluth 1969–1971 at $p \leq 0.05$.
†Statistically significant difference with Duluth 1969–1971 at $p \leq 0.01$.

of Duluth, Minneapolis, and St. Paul during 1969–1971 and Duluth during 1974–1976. Duluth rates during the earlier time period are compared with Minneapolis and St. Paul, and Duluth rates during the later period are compared with rates during the earlier period. Comparisons have been made for 84 primary sites, and those that may be considered at risk of cancer from ingestion of asbestos are presented in the tables.

In the 1969–1971 comparisons, excesses in Duluth that are statistically significant are observed, by sex and primary site, for male peritoneum, retroperitoneum and intra-abdominal; male other peritoneum and digestive; female uterine corpus; and male prostate. In the comparison between the two Duluth time periods, statistically significant increases are observed for female peritoneum, retroperitoneum, and intra-abdominal; female lung cancer; female uterine corpus; and female multiple myeloma. A decrease in male prostate is statistically significant. Data from some of these sites involve very small numbers and must be interpreted with caution even though statistically significant.

Table 4 provides the most recent data for Duluth, for 1979–1980 for males and females separately, again for selected sites. Absolute numbers of cases, average annual crude incidence rates, and SMRs compare Duluth 1979–1980 rates with rates for Duluth 1969–1971 and with the State of Iowa SEER 1973–1977 for whites only. The only statistically significant excesses are Duluth female lung cancer during 1979–1980 in comparison with Duluth rates during 1969–1971, and Duluth male stomach cancer during 1979–1980 in comparison with Iowa SEER 1973–1977. However, the Duluth female lung cancer rate is not statistically significant when compared with that for Iowa, and the Duluth male stomach cancer rate is not statistically significant when compared with that for Duluth 1969–1971.

Table 5 contains the number of cases of pleural and peritoneal malignant mesothelioma in residents of Duluth, by year of diagnosis during

Table 4. Duluth cancer incidence for selected sites during 1979–1980, and standard morbidity ratios.

	Total number		Duluth average annual crude incidence rate 1979–1980[a]		SMR, Duluth 1979–1980[b]		SMR, Duluth 1979–1980[c]	
Primary site	Male	Female	Male	Female	Male	Female	Male	Female
Stomach	18	13	20.5	13.3	0.8	0.9	1.7†	1.6
Colon, excluding rectum	44	50	50.1	51.1	1.1	1.0	1.2	0.9
Rectum and rectosigmoid	19	14	21.6	14.3	1.1	0.7	0.9	0.7
Liver	2	3	4.6	3.1	0.8	1.5	1.0	1.7
Pancreas	6	11	6.8	11.2	0.3	0.6	0.5	0.9
Peritoneum, retroperitoneum and intra-abdominal	1	2	—	—	—	—	—	—
Total gastrointestinal	90	93	102.6	95.0	0.8	0.8	1.0	0.9
Lung and bronchus	64	29	72.9	29.6	0.8	2.3*	0.9	1.5
Pleura	1	0	—	—	—	—	—	—
Prostate	81	—	92.3	—	0.8	—	1.2	—
Female breast	—	93	—	95.0	—	0.8	—	0.9
Bladder	28	11	31.9	11.2	1.2	1.2	1.1	1.0
Kidney and renal pelvis	10	5	11.4	5.1	0.9	0.4	1.2	0.8
All sites combined	364	399	414.8	407.7	0.9	0.9	1.0	0.9

[a]Based on the Duluth 1980 population.
[b]Expected numbers of cancers from application of 1969-1971 Duluth age-sex-specific incidence rates to the 1980 Duluth population.
[c]Expected numbers of cancers from application of the 1973-1977 Iowa white age-sex-specific incidence rates to the 1980 Duluth population.
*Statistically significant at $p < 0.01$.
†Statistically significant at $p < 0.05$.

1969–1980. There were nine cases of pleural and one case of peritoneal during the 12 years of observation. For such a rare disease, it is appropriate to average the number of cases during the study period. This results in an average of 0.75 cases per 100,000 population of pleural mesothelioma occurring per year compared to the observed frequency of 0.2 cases per 100,000 per year in the Minneapolis-St. Paul component of the TNCS. The SMR (9 observed cases, 2.4 expected) of 3.75 is statistically significant at $p = 0.01$ (*16*). An increase in diagnostic surveillance during the mid-1970s, generated from increased concern in this community relative to malignant mesothelioma, may partially account for these differences. Based on the observed frequency of pleural malignant mesothelioma, one would expect approximately one newly diagnosed case per year. In fact, six cases were ascertained during the 3-yr period of heightened concern, 1974–1976, which is double the expected frequency of three.

Table 5. Malignant mesothelioma in residents of Duluth 1969–1980.

	Pleura		Peritoneum	
	Male	Female	Male	Female
1969	—	—	—	—
1970	—	—	—	—
1971	—	—	—	—
1972	—	—	—	—
1973	1	—	—	—
1974	2	1	—	—
1975	1	—	—	—
1976	—	2	—	1
1977	—	—	—	—
1978	1	—	—	—
1979	—	—	—	—
1980	1	—	—	—
Total	6	3	—	1

Discussion

We are unable to explain the variations in rates and the differences that are statistically significant. However, it is clear that rate differences between geographic areas and through time do occur without any apparent biologic reason. Also, in the determination of statistical significance at the $p = 0.05$ level, for every 100 comparisons, 5% will be statistically significant by chance alone. In our opinion, the only statistically significant result with clear biological significance is the increase in female lung cancer in Duluth, undoubtedly a reflection of the increase in cigarette smoking over the past few decades. This increasing trend of lung cancer in women is seen nationally (*14*). The marginally statistically significant excess of stomach cancer in Duluth males, compared with Iowa, is consistent with historical observations of stomach cancer mortality for St. Louis County, the location of Duluth (*17*). The lack of a statistically significant excess in Duluth females, compared with Iowa, is probably due to the smaller number of female cases. Historically, the rates have been high for stomach cancer in males and females long before the occurrence of asbestos exposure. However, the impact of asbestos exposure on the risk of stomach cancer in excess of the risk attributed to known risk factors (i.e., Scandinavian dietary practices) on current cases, cannot be determined (*18*). Other differences of Duluth cancer incidence rates may be important, and a longer time of surveillance coupled with evaluation of mobility and follow-up of the exposed population will need to be conducted before these issues can be resolved.

Needs of Further Research

In my opinion, it will be important to complete the analysis of study period 1969–1981 so that three solid years of data during 1979–1981 around the 1980 census year can be analyzed. At that time, thorough review and analyses of all the data should be conducted. In addition, plans should be made to continue the surveillance, possibly using a modified methodology to accommodate the entire length of exposure of 17 yr and the induction periods of 30–50 yr. Furthermore, the intent of the study design was to incorporate methods for determining length of residency of Duluth cancer cases as a measure of length of exposure and also for determining migration patterns of the exposed population more scientifically than the Census Bureau data currently can permit. A basic problem in study methodology arises in such long-term surveillance when one questions to what degree the observed cancer incidence is measuring the occurrence of disease in the actual exposed population, even for the city of Duluth, which is considered to be a very stable population.

Similar questions also arise for this and other diseases perceived to be environmental threats to human health and yet having very long latent periods. These questions require new methodologies and procedures such as rapidly registering exposed individuals at time of exposure, taking biologic specimens, and incorporating methods of long-term follow-up. Such follow-up would be accomplished much more easily, and scientific study would probably be much more valid if it were possible to use some IRS records and Census Bureau records of individuals in large, exposed populations. Use of those records would greatly enhance and enable long-term follow-up in epidemiologic and biomedical research and would reduce the expense of more difficult and time-consuming follow-up procedures, which are now required (*19*).

It is apparent that there is another major area of needed epidemiologic research regarding the health effects from the ingestion of asbestos in drinking water—the need for development of methods for clinical laboratory studies applied within an epidemiologic design, which would address questions related to low-level dose-response effects, host sensitivity and reactivity for large populations, and the effects of three variables known to affect carcinogenicity of asbestos fibers: the structure, geometry, and surface adsorption characteristics of fibers. Currently, it is difficult to predict the carcinogenic behavior of fibers *in vivo* in both animals and humans.

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